

Applicant(s): Chalifour, et al.
Filing Date: November 5, 2001

REMARKS

Applicant has amended the claims so as to clarify and more particularly indicate the claimed subject matter, and to remove multiple dependencies and informalities. The amendment is made for the sole purpose of expediting prosecution and not in response to any ground or reason of patentability presented by the USPTO. No new matter is added. Accordingly, claims 1-22, 29, 32, and 34-38 are pending in the present application.

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact either of the undersigned at the telephone number provided below.

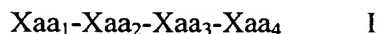
Respectfully submitted,

Ivor R. Elrifi, Reg. No. 39,529
Michel Morency, Limited Recognition
Nicholas P. Triano III, Reg. No. 36,397
Attorneys for Applicant(s)
MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241

Dated: November 5, 2001

Appendix A: marked up version of the claims showing the changes made

1. (amended once) An antifibrillogenic agent for inhibiting amyloidosis and/or for cytoprotection, which comprises a peptide of Formula I, an isomer thereof, a retro or a retro-inverso isomer thereof or a peptidomimetic thereof:



wherein,

Xaa₁ is selected from the group consisting of Lys; and Xaa₅-Lys-;

Xaa₅ is selected from the group consisting of Lys, His-Gln-, His-His-Gln-, Val-His-His-Gln-, Glu-Val-His-His-Gln-, Asp-Asp-Asp-, and Gln-;

Xaa₂ is any amino acid;

Xaa₃ is Val;

Xaa₄ is selected from the group consisting of Phe, Phe-NH₂, Phe-Phe, Phe-Phe-Ala, Phe-Phe-Ala-NH₂, Phe-Phe-Ala-Gln, and Phe-Phe-Ala-Gln-NH₂;

wherein said peptide has at least one [D] amino acid residue,

with the proviso that Lys-Lys-Leu-Val-Phe-Phe-Ala is an all-[D] peptide.

2. The antifibrillogenic agent of claim 1, wherein Xaa₂ is a hydrophobic amino acid residue.

3. The antifibrillogenic agent of claim 1, wherein the peptide of formula I has at least two [D] amino acid residues.

4. The antifibrillogenic agent of claim 1, wherein the peptide of formula I has at least three [D] amino acid residues.

5. The antifibrillogenic agent of claim 1, wherein the peptide of formula I has one [L] amino acid residue.

6. The antifibrillogenic agent of claim 1, wherein the peptide of formula I is an all-[D] isomer peptide.

7. (amended once) The antifibrillogenic agent of claim 1, ~~2, 3, 4, 5, or 6~~, wherein said peptide of Formula I is selected from the group consisting of:

Lys-Ile-Val-Phe-Phe-Ala	(SEQ ID NO:1);
Lys-Lys-Leu-Val-Phe-Phe-Ala	(SEQ ID NO:2);
Lys-Leu-Val-Phe-Phe-Ala	(SEQ ID NO:3);
Lys-Phe-Val-Phe-Phe-Ala	(SEQ ID NO:4);
Ala-Phe-Phe-Val-Leu-Lys	(SEQ ID NO:5);
Lys-Leu-Val-Phe	(SEQ ID NO:6);
Lys-Ala-Val-Phe-Phe-Ala	(SEQ ID NO:7);
Lys-Leu-Val-Phe-Phe	(SEQ ID NO:8);
Lys-Val-Val-Phe-Phe-Ala	(SEQ ID NO:9);
Lys-Ile-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:10);
Lys-Leu-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:11);
Lys-Phe-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:12);
Ala-Phe-Phe-Val-Leu-Lys-NH ₂	(SEQ ID NO:13);
Lys-Leu-Val-Phe-NH ₂	(SEQ ID NO:14);
Lys-Ala-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:15);
Lys-Leu-Val-Phe-Phe-NH ₂	(SEQ ID NO:16);
Lys-Val-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:17);
Lys-Leu-Val-Phe-Phe-Ala-Gln	(SEQ ID NO:18);
Lys-Leu-Val-Phe-Phe-Ala-Gln-NH ₂	(SEQ ID NO:19);
His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:20);
His-His-Gln-Lys	(SEQ ID NO:23); and
Gln-Lys-Leu-Val-Phe-Phe-NH ₂	(SEQ ID NO:24).

8. (amended once) The antifibrillogenic agent of claim 1, wherein the peptide of formula I is a peptide as set forth in SEQ ID NO:2 ~~or SEQ ID NO:3~~.

Applicant(s): Chalifour, *et al.*
 Filing Date: November 5, 2001

9. A labeled conjugate for *in vivo* imaging of amyloid deposits, which comprises a conjugate of formula II:



wherein A is an amyloid plaque-targeting moiety selected from the group consisting of a peptide of Formula I as defined in claim 1, an isomer thereof, a retro or a retro-inverso isomer thereof and a peptidomimetic thereof,

wherein B is a linker portion allowing attachment of the amyloid plaque-targeting moiety to C; and

wherein C is a label that allows for said *in vivo* imaging.

10. The labeled conjugate of claim 9, wherein Xaa₂ in Formula I is a hydrophobic amino acid residue.

11. The labeled conjugate of claim 9, wherein the peptide of formula I has at least two [D] amino acid residues.

12. The labeled conjugate of claim 9, wherein the peptide of formula I has at least three [D] amino acid residues.

13. The labeled conjugate of claim 9, wherein the peptide of formula I has one [L] amino acid residue.

14. The labeled conjugate of claim 9, wherein the peptide of formula I is an all-[D] isomer peptide.

15. (amended once) The labeled conjugate of claim 9, ~~10, 11, 12, 13 or 14~~, wherein said peptide of Formula I is selected from the group consisting of:

Lys-Ile-Val-Phe-Phe-Ala	(SEQ ID NO:1);
Lys-Lys-Leu-Val-Phe-Phe-Ala	(SEQ ID NO:2);
Lys-Leu-Val-Phe-Phe-Ala	(SEQ ID NO:3);
Lys-Phe-Val-Phe-Phe-Ala	(SEQ ID NO:4);
Ala-Phe-Phe-Val-Leu-Lys	(SEQ ID NO:5);
Lys-Leu-Val-Phe	(SEQ ID NO:6);
Lys-Ala-Val-Phe-Phe-Ala	(SEQ ID NO:7);

Applicant(s): Chalifour, et al.
Filing Date: November 5, 2001

Lys-Leu-Val-Phe-Phe	(SEQ ID NO:8);
Lys-Val-Val-Phe-Phe-Ala	(SEQ ID NO:9);
Lys-Ile-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:10);
Lys-Leu-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:11);
Lys-Phe-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:12);
Ala-Phe-Phe-Val-Leu-Lys-NH ₂	(SEQ ID NO:13);
Lys-Leu-Val-Phe-NH ₂	(SEQ ID NO:14);
Lys-Ala-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:15);
Lys-Leu-Val-Phe-Phe-NH ₂	(SEQ ID NO:16);
Lys-Val-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:17);
Lys-Leu-Val-Phe-Phe-Ala-Gln	(SEQ ID NO:18);
Lys-Leu-Val-Phe-Phe-Ala-Gln-NH ₂	(SEQ ID NO:19);
His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-NH ₂	(SEQ ID NO:20);
His-His-Gln-Lys	(SEQ ID NO:23); and
Gln-Lys-Leu-Val-Phe-Phe-NH ₂	(SEQ ID NO:24).

16. The labeled conjugate of claim 15, wherein B is selected from the group consisting of Glucose and Phe.

17. The labeled conjugate of claim 15, wherein C is ^{99m}Tc.

18. (amended once) A method for the treatment of amyloidosis disorders in a patient, which comprises administering to said patient a therapeutically effective amount of a peptide of Formula I as defined in claim 1, ~~2, 3, 4, 5, 6, 7 or 8~~.

19. (amended once) A method for the treatment of amyloidosis disorders in a patient, which comprises administering to said patient a therapeutically effective amount of an antifibrillogenic agent as defined in claim 1, ~~2, 3, 4, 5, 6, 7 or 8~~.

20. (amended once) A composition for the treatment of amyloidosis disorders in a patient, which comprises a therapeutically effective amount of a peptide of Formula I as defined in claim 1, ~~2, 3, 4, 5, 6, 7 or 8~~ in association with a pharmaceutically acceptable carrier.

Applicant(s): Chalifour, *et al.*
 Filing Date: November 5, 2001

21. (amended once) A composition for the treatment of amyloidosis disorders in a patient, which comprises a therapeutically effective amount of an antifibrillogenic agent as defined in claim 1, 2, 3, 4, 5, 6, 7 or 8 in association with a pharmaceutically acceptable carrier.

22. (amended once) A composition for *in vivo* imaging of amyloid deposits, which comprises a therapeutically effective amount of a labeled conjugate as defined in claim 9, 10, 11, 12, 13, 14, 15, 16 or 17 in association with a pharmaceutically acceptable carrier.

23. — Use of a peptide of Formula I as defined in claim 1, 2, 3, 4, 5, 6, 7 or 8 for inhibiting amyloidosis and/or for cytoprotection.

24. — Use of an antifibrillogenic agent as defined in claim 1, 2, 3, 4, 5, 6, 7 or 8 for inhibiting amyloidosis and/or for cytoprotection.

25. — Use of a labeled conjugate as defined in claim 10, 11, 12, 13, 14, 15, 16 or 17 for *in vivo* imaging of amyloid deposits.

26. — Use of a peptide of Formula I as defined in claim 1, 2, 3, 4, 5, 6, 7 or 8 for the manufacture of a medicament for inhibiting amyloidosis and/or for cytoprotection.

27. — Use of an antifibrillogenic agent as defined in claim 1, 2, 3, 4, 5, 6, 7 or 8 for the manufacture of a medicament for inhibiting amyloidosis and/or for cytoprotection.

28. — Use of a labeled conjugate as defined in claim 10, 11, 12, 13, 14, 15, 16 or 17 for the manufacture of a medicament for *in vivo* imaging of amyloid deposits.

29. A peptide, an isomer thereof, a retro or a retro-inverso isomer thereof or a peptidomimetic thereof, for use in inhibiting amyloidosis and/or for cytoprotection, said peptide having a sequence taken from the β -sheet region of an amyloid protein selected from the group consisting of IAPP and protease resistant prion protein.

30. — Use of a peptide as defined in claim 29 for inhibiting amyloidosis and/or for cytoprotection.

31. — Use of a peptide as defined in claim 29 for the manufacture of a medicament for inhibiting amyloidosis and/or for cytoprotection.

32. (amended once) A composition for inhibiting amyloidosis and/or for cytoprotection, which comprises a therapeutically effective amount of a peptide as defined in claim 31, 30 or 31 in association with a pharmaceutically acceptable carrier.

Applicant(s): Chalifour, *et al.*
 Filing Date: November 5, 2001

33. ~~Use of a labeled peptide as defined in claim 29 for the manufacture of a medicament for *in vivo* imaging of amyloid deposits.~~

34. (amended once) A process for the preparation of cells suitable for transplantation into a mammal, which cells are capable of forming amyloid deposits, said process comprising contacting the cells *in vitro* with the peptide of Formula I as defined in claim 1 ~~or with the antifibrillogenic compound as defined in claim 1, 2, 3, 4, 5, 6, 7 or 8 for inhibiting amyloid deposit formation.~~

35. (amended once) ~~Process~~ The process according to of claim 34, wherein said peptide of Formula I or said antifibrillogenic compound causes breakdown of amyloid deposits, the deposits having been formed by said cells prior to said contact.

36. (amended once) ~~The P~~ process according to of claim 34 ~~or 35~~, in which the cells are cultured in the presence of the peptide of Formula I or the antifibrillogenic compound.

37. (new) The antifibrillogenic agent of claim 1, wherein the peptide of formula I is a peptide as set forth in SEQ ID NO:3.

38. (new) A process for the preparation of cells suitable for transplantation into a mammal, which cells are capable of forming amyloid deposits, said process comprising contacting the cells *in vitro* with the antifibrillogenic compound as defined in claim 1 for inhibiting amyloid deposit formation.